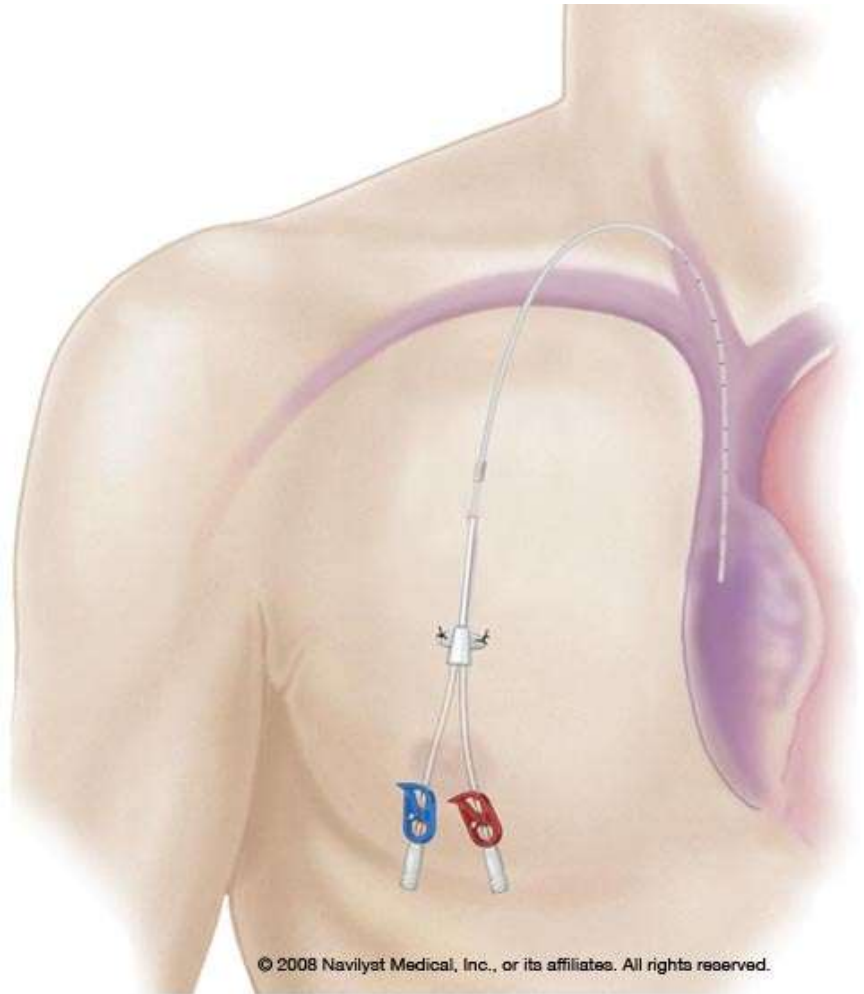

Infection in Patients with Chronic Renal Failure

Nagy A-Hady Sayed-Ahmed
Mansoura University

Dialysis Catheter-Related Infection

Types of catheters

- **Cuffed / non Cuffed.**
- **Luminal design.**
- **Material.**
- **Antiseptic impregnated.**



-
- In 2006, 82% of patients in the United States initiated dialysis via a catheter
 - • The overall likelihood of Tunneled cuffed catheters use was 35% greater in 2005 compared with 1996
-

Prospective study of 526 incident patients starting RRT. 1 year follow up. Univariate analysis:

- The most common single reason for admission was creation of & complications to vascular access for HD.
- The use of temporary vascular access for HD were associated with prolonged hospitalisation & repeated admissions.

Metcalfe Et Al. Q J Med 2003; 96: 899

Septicemia, access and cardiovascular disease in dialysis patients

- ➡ First cause of Morbidity.
- ➡ Second cause of mortality

shani A, Collins AJ, Herzog CA, Foley RN: Kidney Int 68: 311–318, 2005

Indication of catheter

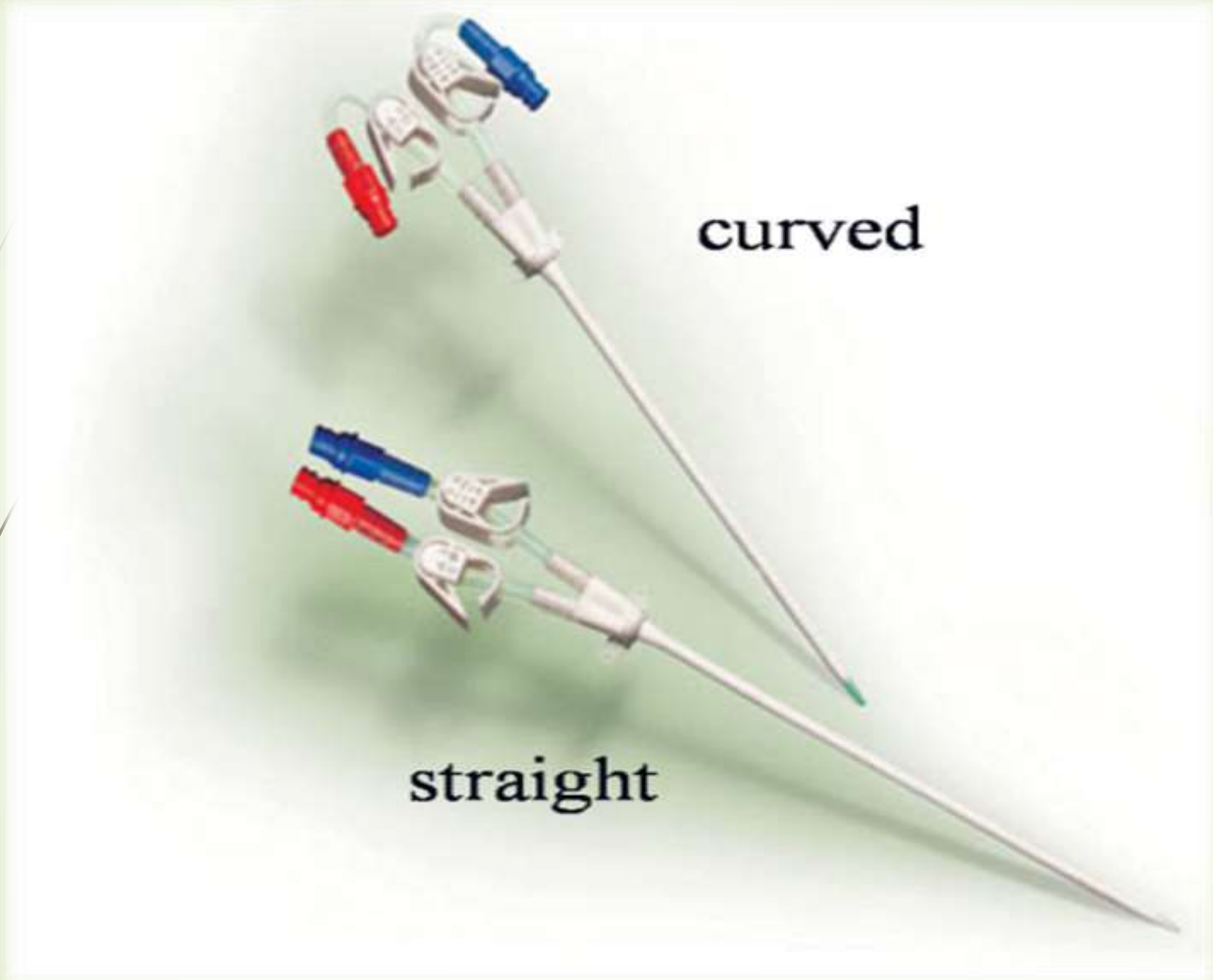
- Acute Kidney Injury .
- ESRD with no access.
- ESRD with failure of access.
- Peritoneal dialysis with complications.
- Transplant patients require HD.
- Plasmapheresis and Hemoperfusion.
- Dialysis for overdose.

Types of catheters

Temporary non Cuffed Catheters

- Short.
- More ridged.
- Easy and fast insertion.
- Immediate use.
- Higher infection rate.
- Preferred IJ or femoral.
- Avoid subclavian.
- < 3wks for IJ.
- <5 days for femoral.

Temporary non Cuffed Catheters



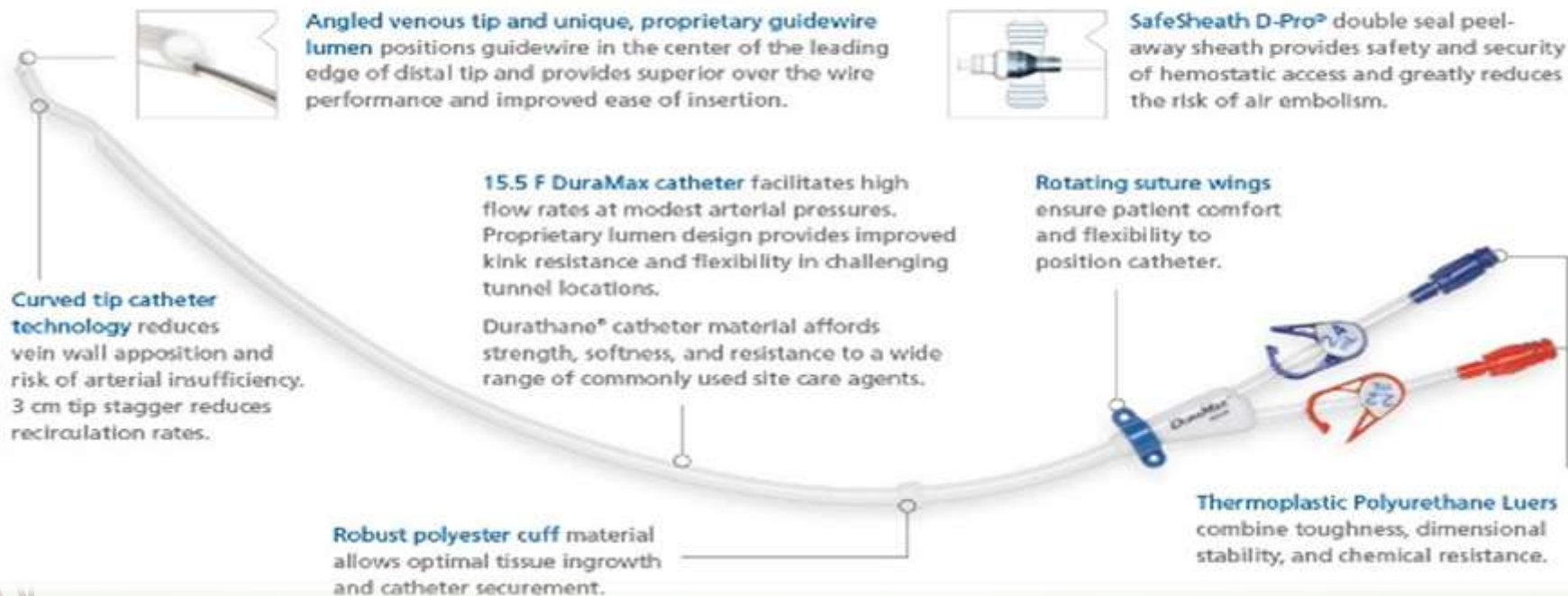
Types of catheters

Cuffed Tunneled Catheters

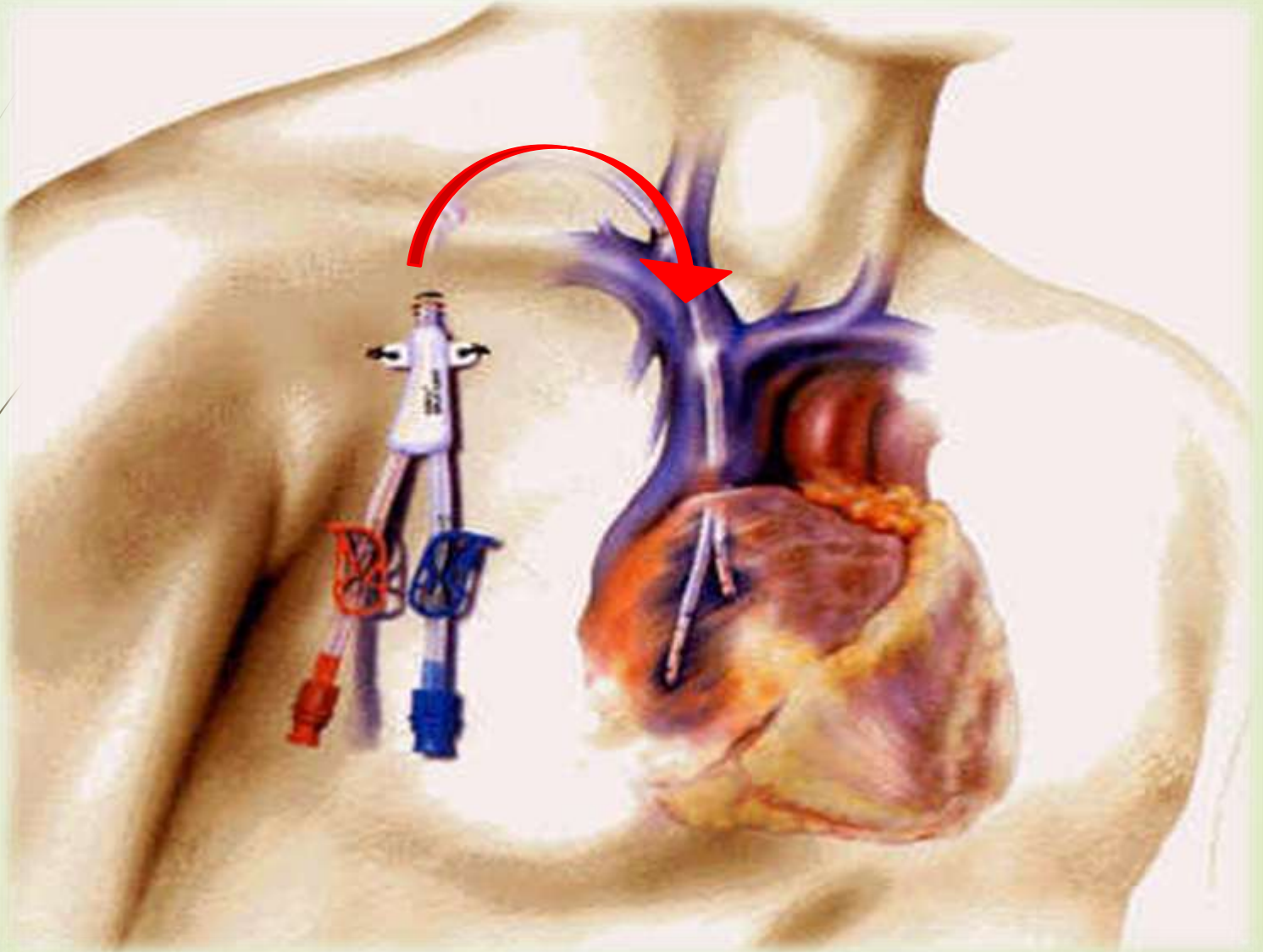
- Dacron cuff.
- Softer.
- Sheath for insertion.
- Different holes, length and material.
- Requires sedation.
- Lower neck insertion site.
- More bleeding.
- **1 year –Indefinite.**

Cuffed Tunneled Catheters

DuraMax[®] *Engineered for Excellence[™]* CHRONIC DIALYSIS CATHETER



Cuffed Tunneled Catheters



Pathogenesis

- ?? all indwelling vascular catheters are colonized by microorganisms
- micro organisms imbedded in a biofilm layer and can be present 24h after insertion .
- a link between the No of organisms by culture and the risk of infection associated with these catheters
- Infection depend on whether the organism on the catheter surface exceed a certain quantitative threshold.

Source of infections

- Organisms enter the bloodstream from the skin insertion site or through the hub of the catheter.
- introduced into the hub of catheter by hands of medical personnel.
- Skin organisms migrate from the skin insertion site along the external surface of the catheter colonizing the intravascular tip.
- The subsequent colonization of the internal surface of catheter cause blood stream infection.

Causative organisms

Organism	Percentage reported
Gram-positive cocci	52 – 85 %
Staphylococcus aureus	22 – 60 %
Staphylococcus epidemics	9 – 13 %
Meticillin-resistant Staphylococcus aureus	6 – 29%
Enterococcus faecalis	2 – 18 %
Gram-negative bacilli	20 – 28 %
Pseudomonas aeruginosa	2 – 15 %
Enterobacter cloacae	9 %
Escherichia coli	10 %
Acinetobacter species	13 %
Serratia marcesens	1 – 2 %
Klebsiella pneumonia	6 %
Polymicrobial	16- 20 %
Acid-fast organisms	Rare
Fungi	Rarely reported

Types of HD catheter infection

- Localized exit site infection.
- Tunnel infection.
- Systemic infection.
- Last access cuffed tunneled infected catheter.

Rate of hemodialysis catheter infection

Rate of uncuffed cath. infection:

- 8% by 2wks.
- 25% by 1 month.
- 50% by 2 months.
- Catheter related septicemia is 2 -20%.

Agarwal, Anil K, Asif Arif. NephSAP. Interventional Nephrology, ASN. 361-375. 2009.

- Cuffed rate 1.6-5.5/1000 d.
- Non cuffed 3.8-6.6/1000 d.

Beathard GA, Urbanes A: Infection associated with tunneled hemodialysis catheters. Semin dial 21: 528-538, 2008.

Predisposing factors

Host- related factors

Pathogen related factors

Catheter related factors

Hemodialysis procedure-related factors



Host- related factors

- Impaired host immunity
- Poor personal hygiene
- Occlusive dressing
- *S. aureus* nasal carriage older age
- Diabetes mellitus
- Recent hospitalization
- High cumulative dose of intravenous iron

Pathogen related factors

- Biofilm formation
- Resistance to antibiotic therapy
- Bacterial virulence
- *S. aureus* nasal carriage
- Contiguous infection

Catheter related factors

- Site of insertion
- Increased duration of catheter use
- History of bacteremia
- Colonization of catheter tip and cutaneous tract with skin flora
- Catheter lumen contamination
- Hematogenous seeding of the catheter from another infectious source
- Contamination of the lumen with infusate
- Lack of aseptic precautions during catheter insertion



Hemodialysis procedure-related factors

- Inadequate water treatment
- Contamination of dialysate or equipment
- Dialyzer reuse

Hemodialysis Catheter infection complications

- Serious complications, including infective endocarditis, septic arthritis, septic emboli, osteomyelitis, epidural abscess and severe sepsis, have been reported in 20% of cases
- *S. aureus* has been predominantly isolated from those patients as a result of the predilection of *S. aureus* for heart valves and bone

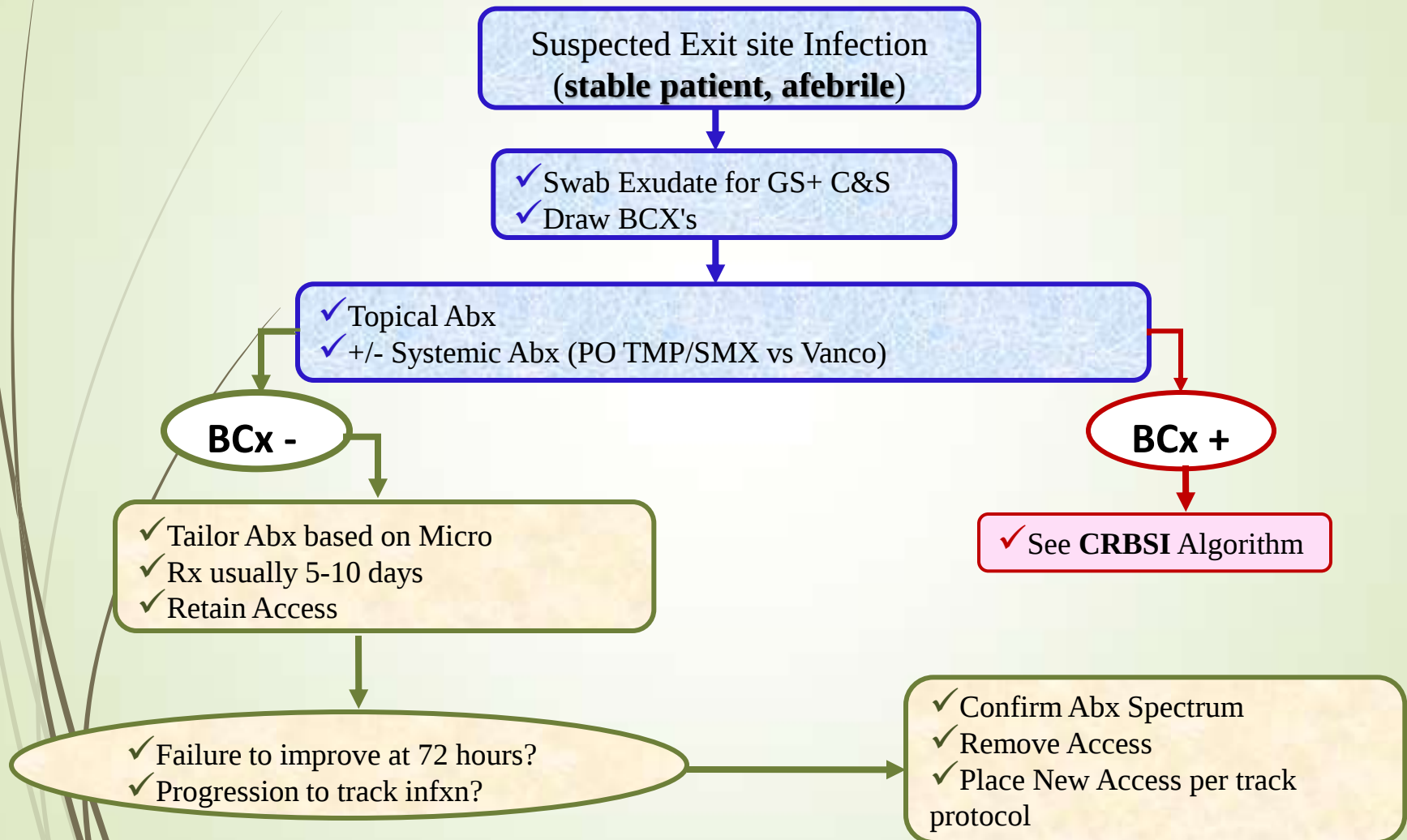
Investigations for catheter infection

- ➡ CBC.
- ➡ Exit site & discharge Cx
- ➡ Blood Culture peripheral and from catheter.
- ➡ Catheter tip Cx.
- ➡ Others: Urine, Sputum, Drains..etc.

Exit site infection

- Erythema, discharge and tenderness.
- Obtain Cx.
- Could be treated with Local and oral AB.
- Rarely required removing the catheter.

Algorithm for Suspected Exit Site Infections



ESNT Vascular Access Guidelines



Guideline 5.3 – Minimizing the risk of catheter related infection

- We recommend that the catheter exit site should be cleaned with Chlorhexidine 2%. (1B)

ESNT Vascular Access Guidelines

We recommend application of either topical agents or intraluminal lock solutions for the reduction of exit-site infection and catheter-related bacteraemia.

Options of topical agents include mupirocin 2% ointment and polysporin. Intraluminal lock agents include both antibiotic based and non-antibiotic-based solutions.

(Level 1 evidence)

Catheter Tunnel infection

- Inflammatory signs over the tunnel.
- Purulent discharge.
- IV AB.
- Exchange of the catheter.
- Different site.

Algorithm for Suspected Track Infections

Suspected Tunnel Infection
(**stable patient, afebrile**)

- ✓ Swab Exudate for GS+ C&S
- ✓ Draw BCX's
- ✓ Remove Line ASAP (<24hours)
- ✓ Establish PIV(not PICC if possible)

IV Vanco + [tobra or ceftaz]

BCx -

- ✓ Tailor Abx based on Micro
- ✓ Rx usually 5-10 days

Ideal criteria for new access?

- ✓ 48 hours appropriate abx
- ✓ 48 hours BCx-negative
- ✓ Non-infected track tissue available

BCx +

- ✓ See **CRBSI** Algorithm

Catheter related Bacteremia

Clinical picture:

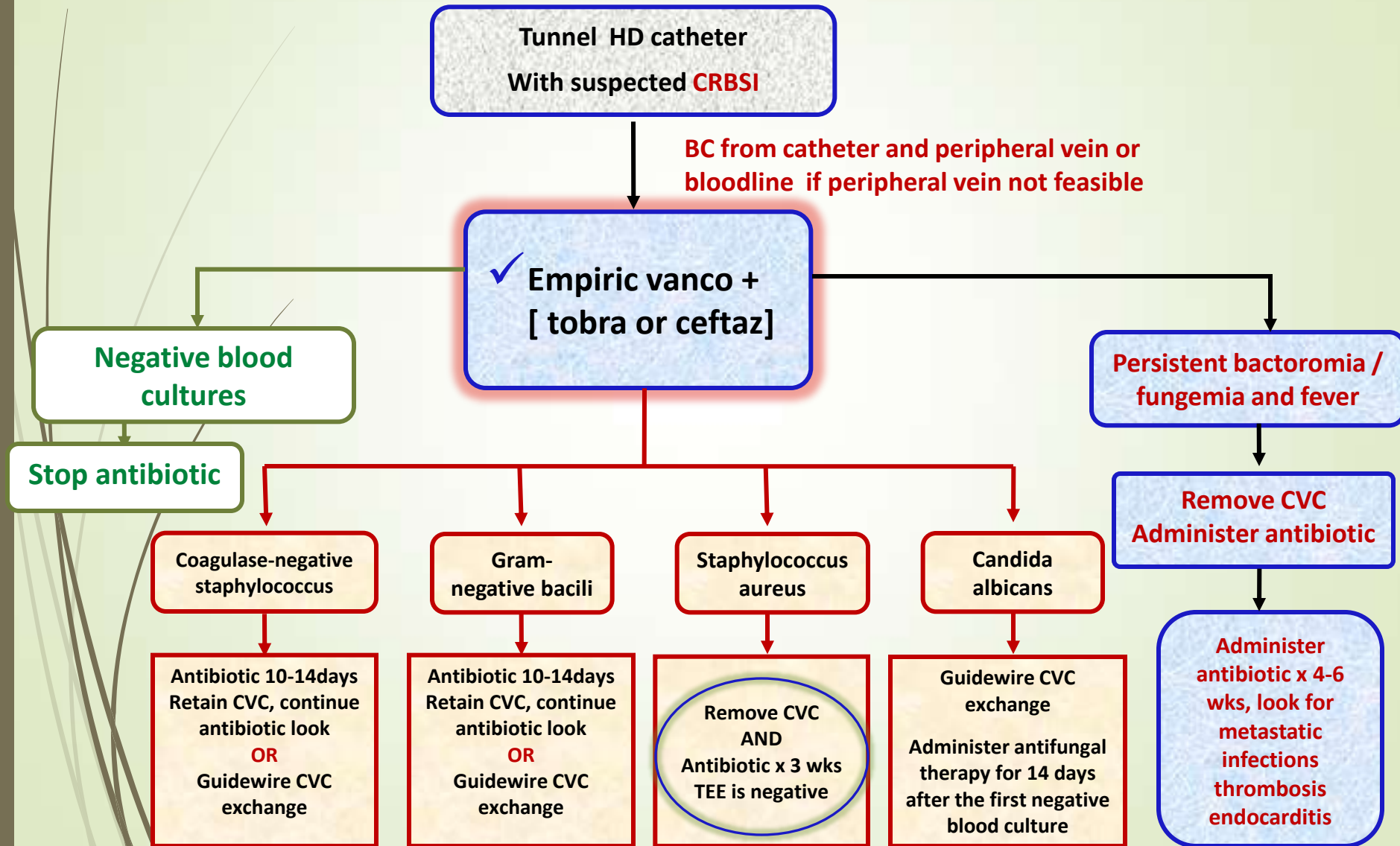
- Fever with chills.
- May be only during HD.
- patient with Central catheter.
- No other focus of sepsis.

Dx: Blood Cx > 15CFU. From peripheral and catheter

Treatment AB for 2-3 wks with exchange of the catheter

The catheter is the cause of fever unless proven otherwise

Algorithm for Suspected catheter related bacteremia (CRBSI)



Indications for catheter removal

- Unstable patients
- Bacteremia with tunnel involvement
- Metastatic infection.

ESNT Vascular Access Guidelines



Guideline 6.1 – Treatment of access infection and related bacteremia

- We recommend that venous catheters should be removed in all seriously ill hemodialysis patients with catheter related bacteremia unless no alternative vascular access can be achieved. (1B)

Criteria to attempt catheter salvage

- Difficult to replace catheters
 - A hemodynamically stable patient
 - Blood sterile in 48–72 h
 - No sign of tunnel infection
 - No signs of metastatic infection
 - Microorganisms medically treatable
-
- There is a 5-fold higher risk of treatment failure when TCC salvage is attempted, and an 8-fold higher risk in cases associated with *S. aureus* bacteraemia
 - Salvage should be used only as a treatment of last resort

Catheter Salvage in poor access

30% AB treatment could clear infection.

80% AB with exchange over guide wire.

Tanriover B, Carlton D, Saddekni S, Hamrick K, Oser R, Westfall AO, Allon M: Bacteremia associated with tunneled dialysis catheters: Comparison of two treatment strategies. Kidney Int 57: 2151–2155, 2000

Exchange:

- 72 hours post AB.
- No need for negative blood Cx.

National Kidney Foundation: KDOQI clinical practice guidelines and clinical practice recommendations for vascular access 2006. Am J Kidney Dis 48[Suppl 1]: S176–S322, 2006

Antibiotic Lock

- Is indicated in reinfection with same organism.
- In limited catheter sites.
- Catheter Salvage is acceptable.

Onder AM, Chandar J, Simon N, Diaz R, Nwobi O, Abitbol CL, Zilleruelo G:
Nephrol Dial Transplant 23: 2604–2610, 2008.

ESNT Vascular Access Guidelines



Guideline 5.4 – Minimizing the risk of catheter related infection

- ➡ We suggest that an antimicrobial or antibiotic lock solution be used to reduce catheter related bacteremia and other infections. (2B)

Electronic Nephrology Education: ESNT Virtual Academy

Types of Antibiotic Lock

➤ Cefazolin, Cephalexin, Vancomycin, Tobramycin, Gentamicin.

Concentration: 5mg/ml.

mixed with Citrate, EDTA, Heparin

Systemic AB with Antibiotic lock more effective for

- G. Neg.
- Less effective for Staph. Epidermidis.
- Worst for Staph aureus.

Conclusion

- Strict follow up infection control policy in insertion and manipulations of dialysis catheters .
- Update the National guidelines
- Dialysis Access Care program
- More efforts in Patient education
- AVF First

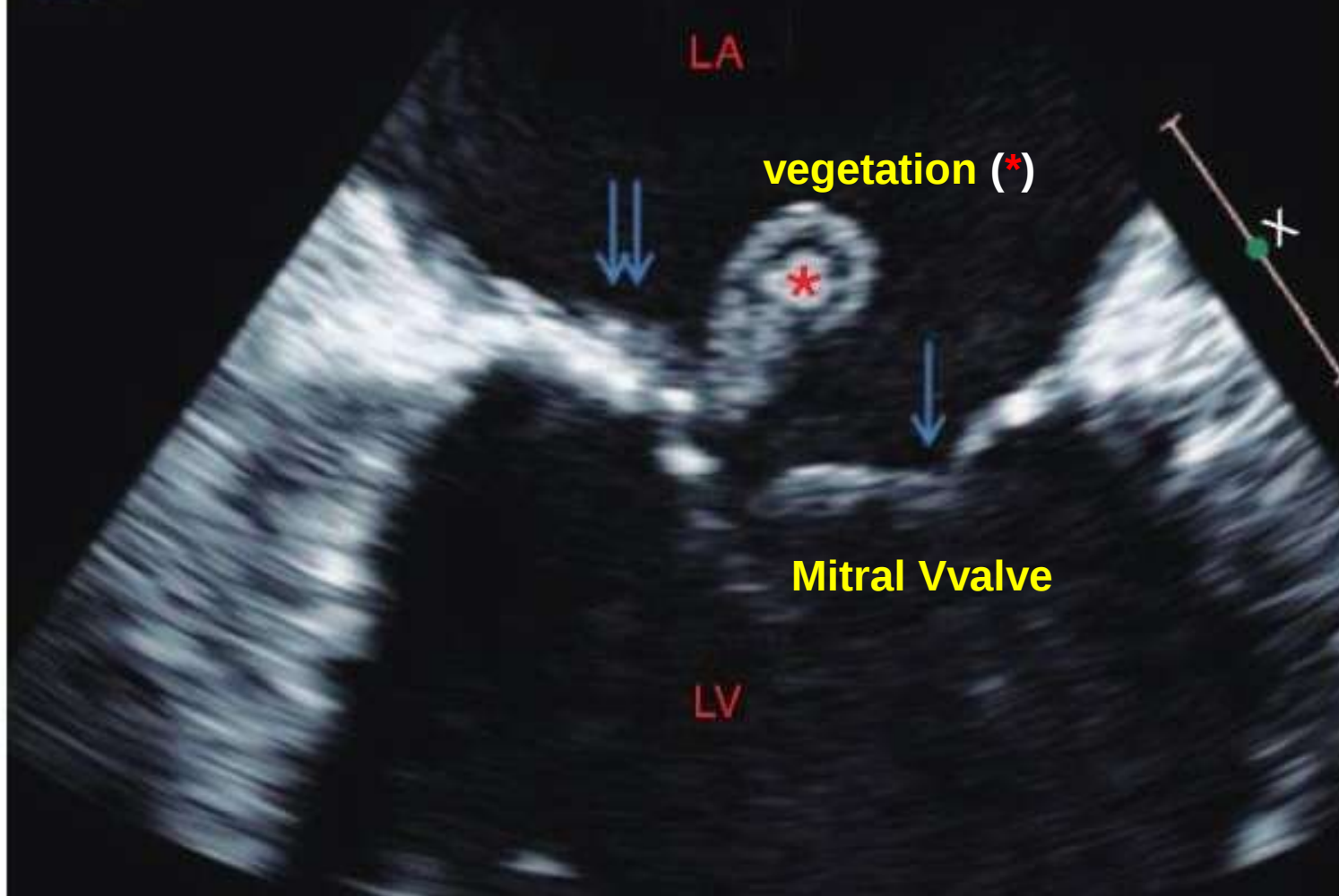
Exit site infection

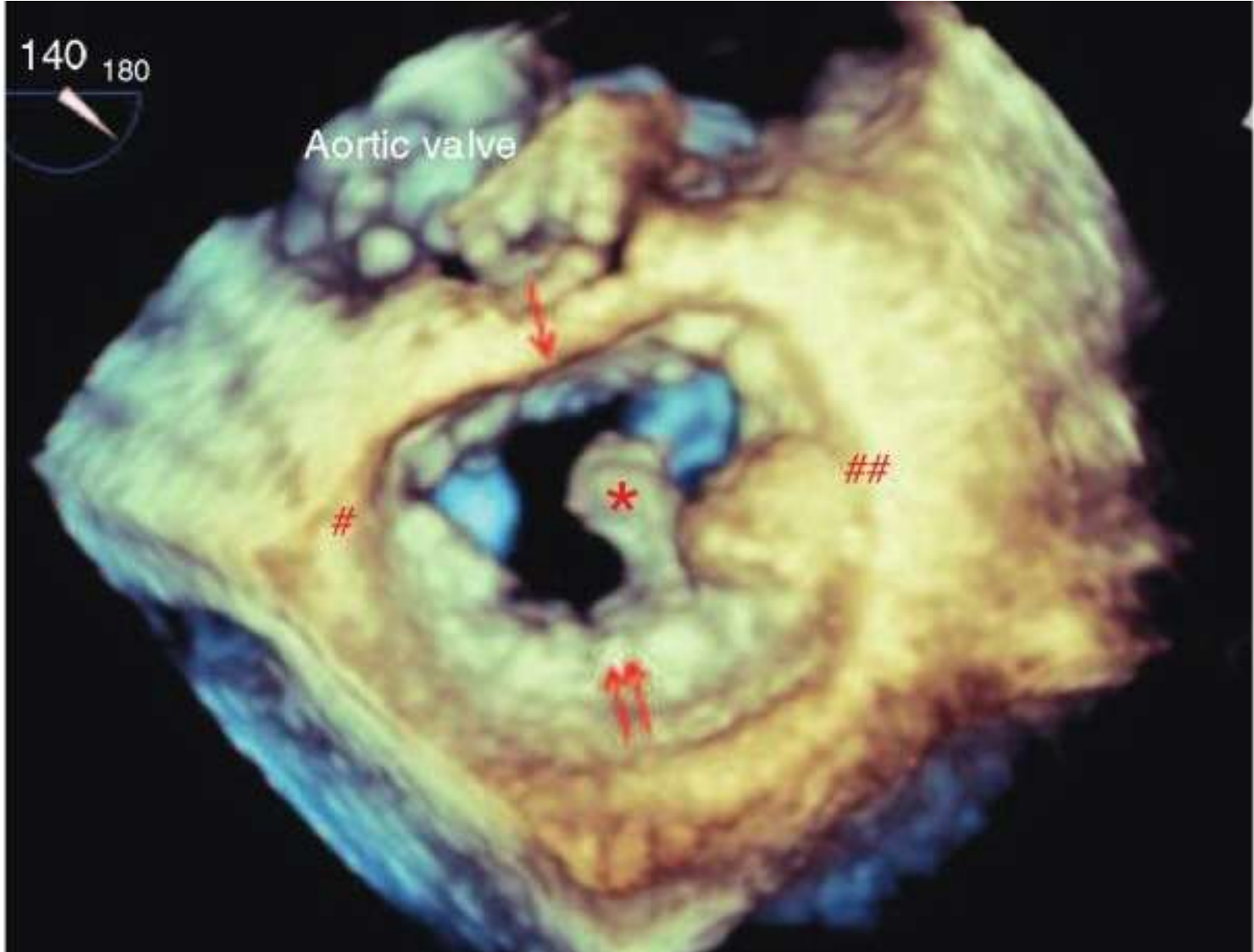




TE Echo

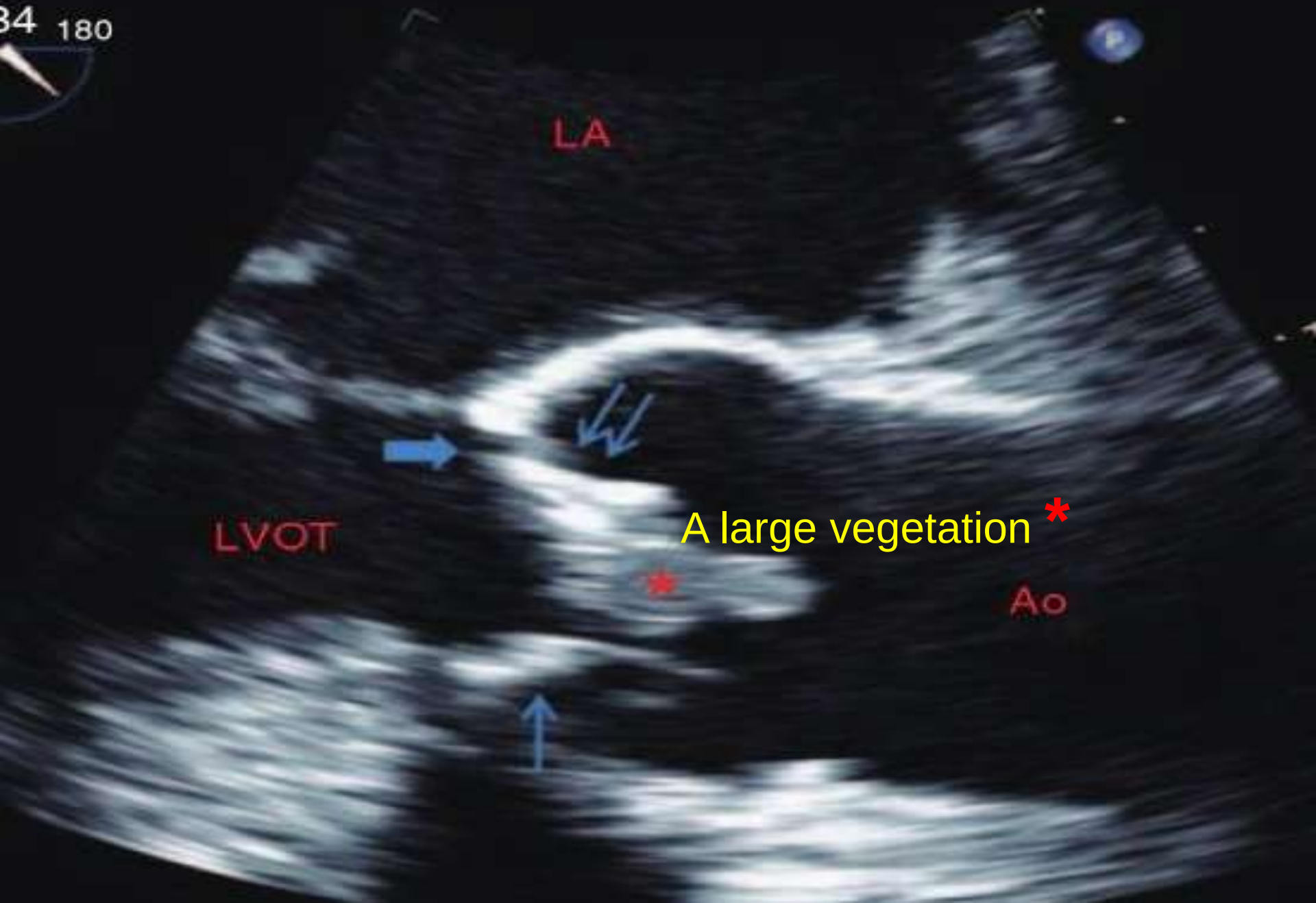
79 180





Three-dimensional TE echo image of the open mitral valve ('surgeon's view'). A large vegetation (*) is seen

Two-dimensional TE echo image of the aortic valve



Measures during catheter manipulations aimed at reducing catheter-related bloodstream infections – 1

- All catheter manipulations should be done by specifically trained personnel
 - Catheter exit site should be examined and dressings renewed at each dialysis session
 - During all procedures that include catheter cap or catheter dressing removal the patient should wear surgical mask or face shield and personnel should wear surgical mask or face shield and sterile gloves
-

Measures during catheter manipulations aimed at reducing catheter-related bloodstream infections – 2

- Manipulation of the catheter or accessing the bloodstream should be done in a manner that minimizes contamination, therefore:
 - ❑ catheter hub and bloodline connectors should be cleaned using povidone iodine
 - ❑ catheter lumen should not be left open to the air, place cap or syringe on catheter
 - ❑ catheter lumen should be kept sterile
-



UTI in CKD

UTI in Pts with CKD

- ?? the frequency of UTI in pts with CKD is not known to be different from that in the general population
 - ?? the chronic disease that causes the renal insufficiency could ↓ the risk for UTI due to ↓ risk factors e.g. sexual activity
 - ?? The risk might ↑ by disease factors (e.g., papillary necrosis, nephrolithiasis, neurogenic bladder) and the management of comorbidities with Foley catheters and i.v. lines
-

Microbiological Spectrum of UTIs

- due to the same urinary pathogens as those found in the general population
- the majority of ascending infections being caused by *E.coli*
- *Proteus spp.*, *Enterobacter spp.* and *Enterococcus faecalis*. *Klebsiella pneumoniae* and group B streptococci
- fungi, particularly *Candida species* (*C. albicans*, *C. glabrata*, *C. tropicalis*).

Causative organisms and treatment of urinary tract infection in patients with diabetes – 1

Infection	Common Organisms	Antimicrobial Therapy	Further Management and Comments
Acute bacterial cystitis	<i>E. coli</i> , <i>Proteus species</i>	Trimethoprim 200 mg 2x	Early surgical intervention in emphysematous infection
		Ciprofloxacin 500 mg 2x	Consider ESBL if no clinical improvement
Acute pyelonephritis	<i>E. coli</i> , <i>Proteus species</i>	Ciprofloxacin 500 mg/400 mg 2x or 3 rd gen. cephalosporins or piperacillin/tazobactam 4.5 g3x 7–14-day course	Emphysematous infection should be considered
		If ESBL suspected meropenem 500 mg/1 g3x	

Causative organisms and treatment of urinary tract infection in patients with diabetes – 2

Infection	Common Organisms	Antimicrobial Therapy	Further Management and Comments
Emphysematous pyelonephritis	<i>E. coli</i> , <i>K. pneumoniae</i>	As above	Emergency nephrectomy often required
Perinephric and intra-renal abscess	<i>E. coli</i> and other Gram-negative bacilli (associated with pyelonephritis)	As above but consider adding flucloxacillin 1 g/2 g i.v. if <i>S. aureus</i> suspected	Surgical drainage

Causative organisms and treatment of urinary tract infection in patients with diabetes – 3

Infection	Common Organisms	Antimicrobial Therapy	Further Management and Comments
Fungal cystitis	Candida species (<i>C. albicans</i> , <i>C. glabrata</i> , <i>C. tropicalis</i>)	Fluconazole 100 mg ^{2x} 7–14 days (Amphotericin B bladder irrigation or single dose i.v. amphotericin)	Removal of urinary catheter
Fungal pyelonephritis and abscesses	Candida species (<i>C. albicans</i> , <i>C. glabrata</i> , <i>C. tropicalis</i>)	Fluconazole 6 mg/kg/day prolonged therapy (2–6 weeks) or i.v. amphotericin	Surgical drainage Removal of stents and relieve obstruction if any

Drug	Dose, Route	Excretion <i>via</i>	Peak Serum Concentration (µg/ml)	% Renal Excretion of Unchanged Drug	Urine Concentration (µg/ml)
β-Lactams					
ampicillin	0.5 g p.o.	GF, TS	3 to 6	75 to 92	1000 to 2250
amoxicillin	0.5 g p.o.	GF, TS	6 to 10	60 to 98	300 to 1300
aztreonam	1 g IV	GF, TS	125	65 to 94	1000 to 5000
piperacillin	3 g IV	GF, TS	209	74 to 89	8000
ticarcillin	3 g IV	GF, TS	257	80 to 99	650 to 2500
cephalexin	1 g p.o.	GF, TS	32	91 to 100	5000 to 10,000
cefuroxime	1 g p.o.	GF, TS	14	50	1000 to 7000
cefixime	0.2 g p.o.		1 to 4	20 to 50	
cefdinir	0.3 g p.o.		1.6	18	21 to 139
cefpodoxime	0.2 g p.o.		2.3	29 to 33	20
cefazolin	1 g IV	GF, TS	188	90 to 96	700 to 2000
ceftriaxone	1 g IV	GF	130	65 to 95	549 to 995
imipenem	0.5 g IV	GF, TS	21 to 58	5 to 42	500
meropenem	1 g IV	GF, TS	50	62 to 83	N/D
ertapenem	1 g IV		154	38	N/D
Fluoroquinolones					
ciprofloxacin	0.5 g p.o.	GF, TS	1.6 to 2.9	30 to 50	350
gatifloxacin	0.4 g p.o.		4.2	65	N/D
gemifloxacin	0.320 g p.o.		0.7 to 2.6	<35	N/D
levofloxacin	0.5 g p.o.	GF	5.7	61 to 86	286
moxifloxacin	0.4 g p.o.		4.5	20	N/D
Miscellaneous					
nitrofurantoin	0.1 gm p.o.	GF, TS, TR	<2	27 to 56	50 to 200
trimethoprim	0.16/0.8 g p.o.		9/105	50 to 75/10 to 30	31 to 165/10 to 133
sulfamethoxazole					
trimethoprim	0.2 gm p.o.	GF, TS	2	50 to 75	70 to 100
sulfamethoxazole	0.8 g p.o.	GF, TS, TR	46	N/D	400 to 2000
Aminoglycosides					
amikacin	0.5 g IV	GF, TR	17 to 25	>90	170 to 1720
gentamicin	0.08 g IV	GF, TR	4 to 8	>90	400 to 500
tobramycin	0.08 g IV	GF, TR	4 to 8	>90	94 to 443

Issues for antimicrobial efficacy in UTI – 1

- High urine drug concs. are necessary to sterilize urine
- For pyelonephritis, it is necessary to have effective tissue concs. of the antimicrobial agent
- The serum concs. of anti-infectives correlate with the drug conc. in renal tissue
- **Glomerular filtration $\pm$ net tubular secretion determines urine conc. of drugs**

Issues for antimicrobial efficacy in UTI – 2

- Renal insufficiency + therapeutic serum drug levels + adequate arterial perfusion of the renal parenchyma: → the delivery of therapeutic drug concs. to both the parenchyma and the urine **should not be a problem.**
- Renal insufficiency + cystitis: → there is a possibility that the urine drug conc. **may be too low** to eradicate the etiologic organism.

Issues for antimicrobial efficacy in UTI – 3

- Reports indicate an inferior performance of Amox-Clav as compared with ciprofloxacin in the treatment of uncomplicated cystitis in women
- none of the 4 oral cephalosporins listed has Food and Drug Administration approval for UTI
- Cefazolin and ceftriaxone achieve very high urine concentrations
- Imipenem and ertapenem are approved for the treatment of UTI, whereas **meropenem is not**

Issues for antimicrobial efficacy in UTI – 4

- Gemifloxacin and Moxifloxacin have low urine concs. and are **not indicated** in the treatment of UTI in patients with normal or abnormal renal function
 - Ciprofloxacin and Levofloxacin achieve high urine concs. with oral or parenteral therapy
 - **Nitrofurantoin**: Patients with GFR <20 ml/min excrete little or no drug in the urine
-

Issues for antimicrobial efficacy in UTI – 5

- Trimethoprim-sulfamethoxazole:
 - ❑ increasing documentation of resistance of *E. Coli* - resistance in the range of 15 to 35%
 - ❑ urine concs. of sulfamethoxazole ↓ to subtherapeutic concs. in patients with GFR <50 ml/min
- Urine trimethoprim conc. remains high even with marked renal insufficiency:
 - ❑ prescribe trimethoprim alone, in reduced dosage, for the treatment of uncomplicated cystitis in patients with a low creatinine clearance

Issues for antimicrobial efficacy in UTI – 6

- Aminoglycosides are not indicated for the treatment of cystitis or urethritis:
 - ❑ At present, *E. coli*, *Klebsiella* species, and other common Gram-negative causes of pyelonephritis are susceptible to fluoroquinolones and extended-spectrum β -lactam antibiotics, making unnecessary the use of potentially toxic aminoglycosides
 - ❑ Rarely, it might be necessary to use aminoglycosides in low synergistic doses in combination with an active penicillin for enterococcal pyelonephritis
 - ❑ Adjustment of dosage should yield effective serum and renal parenchymal levels and adequate urine concs., lower the risk for further drug-induced renal injury, and minimize the chance of ototoxicity

Acute Effects of Urinary Tract Infection (UTI) on the Kidney

- In acute pyelonephritis, very dramatic changes can occur with
 - focal reduction in perfusion on imaging and corresponding renal tubular dysfunction.
- However, if in the adult the kidney is normal beforehand, chronic renal damage is most unlikely.
 - There is no evidence that more prolonged or intensive antibiotic treatment of acute pyelonephritis will shorten the episode or prevent complications.

In diabetes mellitus

- overwhelming infection can predispose to pyogenic infection with intrarenal perinephric abscess formation, emphysematous pyelonephritis, and, very rarely, a specific form of infective interstitial nephropathy.
- Papillary necrosis is a common consequence of pyelonephritis in diabetics.
- Females are more prone to asymptomatic bacteriuria than diabetic men, but in both sexes progression to clinical pyelonephritis is more likely than in normal individuals.
- The risk factors for developing asymptomatic bacteriuria differ between type I and type II diabetes.
- It is arguable that diabetic patients are susceptible to rapid progression of parenchymal infection. However, the clearance of asymptomatic bacteriuria should not be attempted if the intention is to prevent complications, notably acute pyelonephritis (**A**).

Chronic Renal Disease and UTI

- Predisposing Factors: **loss of several urinary defense mechanisms and a degree of immunosuppression**.
- Typically, APCKD, gross vesicoureteric reflux (VUR) and endstage obstructive uropathy will harbour infective foci or promote ascending infection, but not invariably so.
- Clearly, severe UTI can ↑ progression of renal failure,
 - **Little evidence that vigorous treatment of lesser degrees of infection or prophylaxis will slow renal functional impairment once it is established (C).**
- In patients with VUR and UTI in endstage chronic renal failure, **bilateral nephroureterectomy** should only be undertaken as a last resort (**B**).

Adult Polycystic Kidney Disease (APCKD)

- In patients with acute pyelonephritis and infected cysts (presenting as recurrent bacteraemia or 'local sepsis')
 - **Treatment requires a long course of high-dose systemic fluoroquinolones, followed by prophylaxis.**
 - **Bilateral nephrectomy should be utilized as a last resort (B).**

Use of Antibiotics for UTI with Renal Impairment

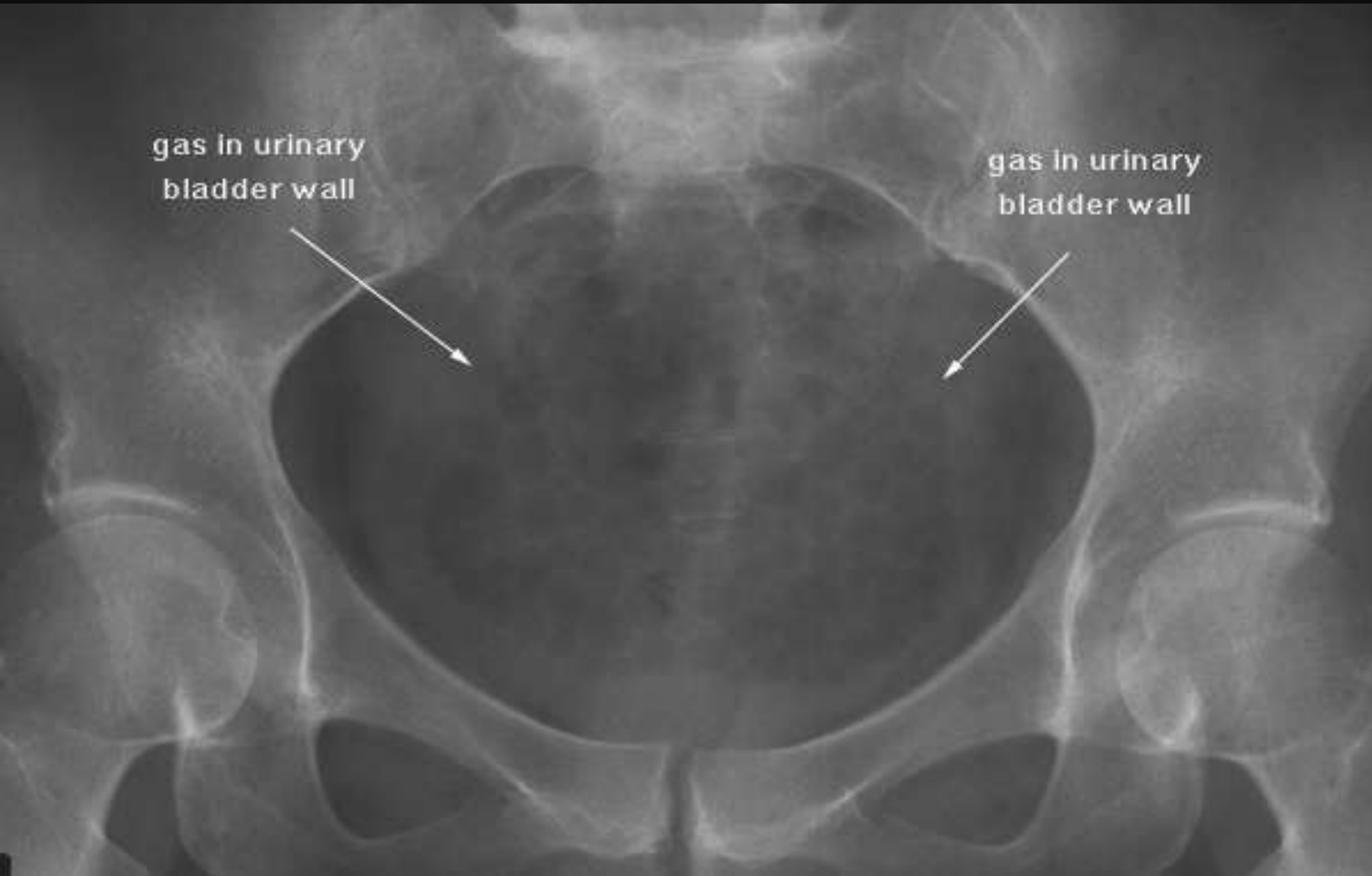
- Most antibiotics have a wide therapeutic index.
 - No adjustment of dose is necessary until GFR <20 mL/min, except antibiotics with nephrotoxic potential (e.g., aminoglycosides).
- Drugs removed by HDx should be administered after a HDx treatment.
- Combination of loop diuretics (e.g., furosemide and a cephalosporin) is nephrotoxic.
- Nitrofurantoin and tetracycline: contraindicated, but not doxycycline.

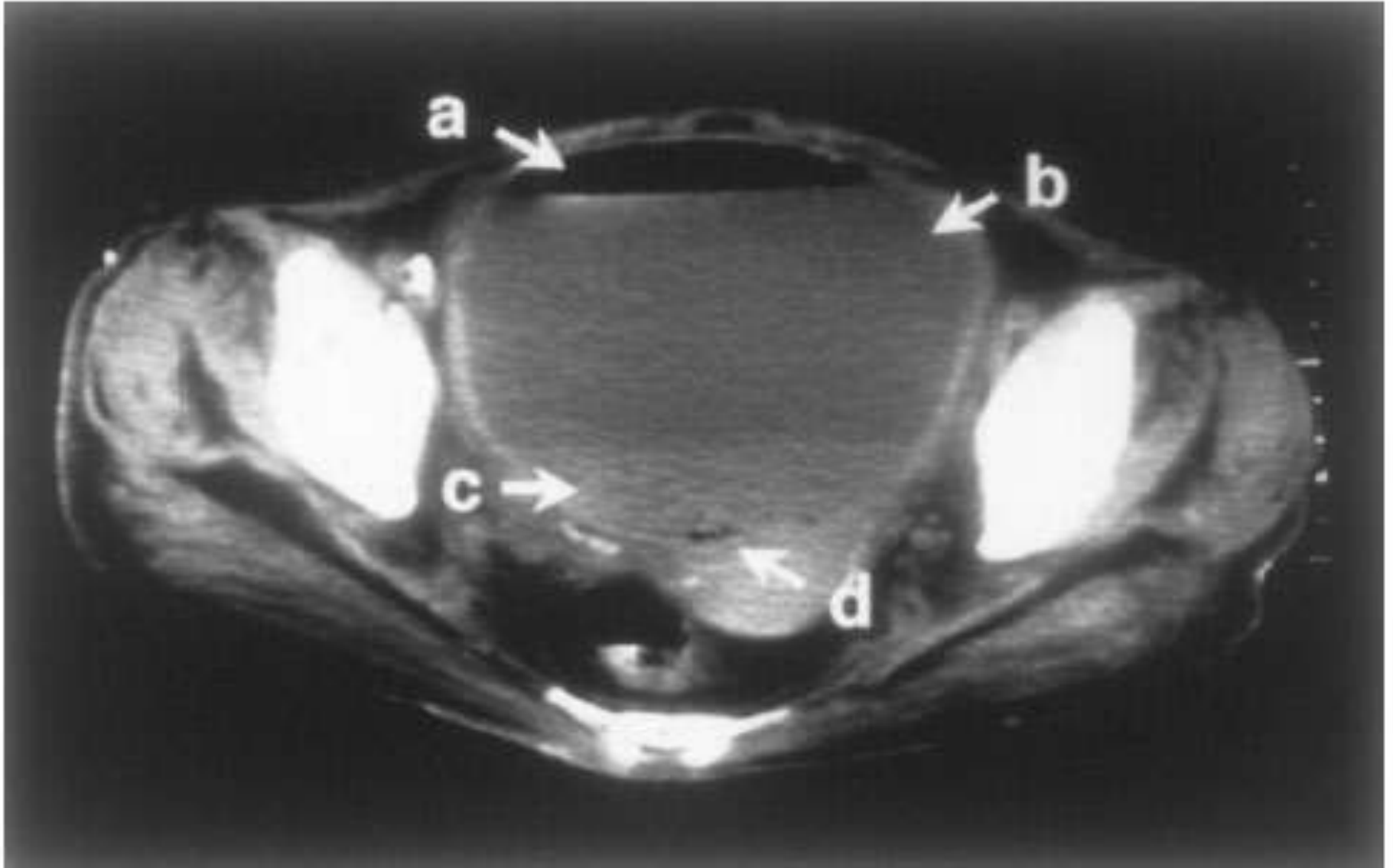
Clearance of Antibiotics at Haemodialysis

Dialyzed	Slightly Dialyzed	Not Dialyzed
Amoxycillin/ampicillin	Fluoroquinolones*	Amphotericin
Carbenicillin	Co-trimoxazole	Methicillin
Cephalosporins*	Erythromycin	Teicoplanin
Aminoglycosides*	Vancomycin	
Trimethoprim		
Metronidazole		
Aztreonam*		
Fluconazole*		

*Drugs cleared by peritoneal dialysis.

KUB demonstrates emphysematous cystitis with gas in the urinary bladder wall





Abdominal CT Scan: remarkable expansion of UB with
a) Gas, b) Urine, c) blood & debris – Emphysematous
Cystitis



CT Scan shows a hydroaeric level and a pneumobladder



Plain abdominal radiography showed air throughout the urinary tract in the kidneys, ureters, and bladder (arrows). Laboratory data: BG 519 mg/dL, CRP 37.1 mg/L, serum creatinine 1.6 mg/dL. CBC: WBC 11.9×10^3 /cubic millimeter.

acute emphysematous cystitis

Emphysematous Pyelonephritis – 1

- A rare, life-threatening condition, usually occurring in diabetic patients
- First described in 1898, an acute necrotizing parenchymal and perirenal infection caused by gas forming uropathogens
- Diabetics account for 70–90% of all cases
- Patients are typically very ill with circulatory/liver failure caused by sepsis
- in 10% of cases, the condition is bilateral

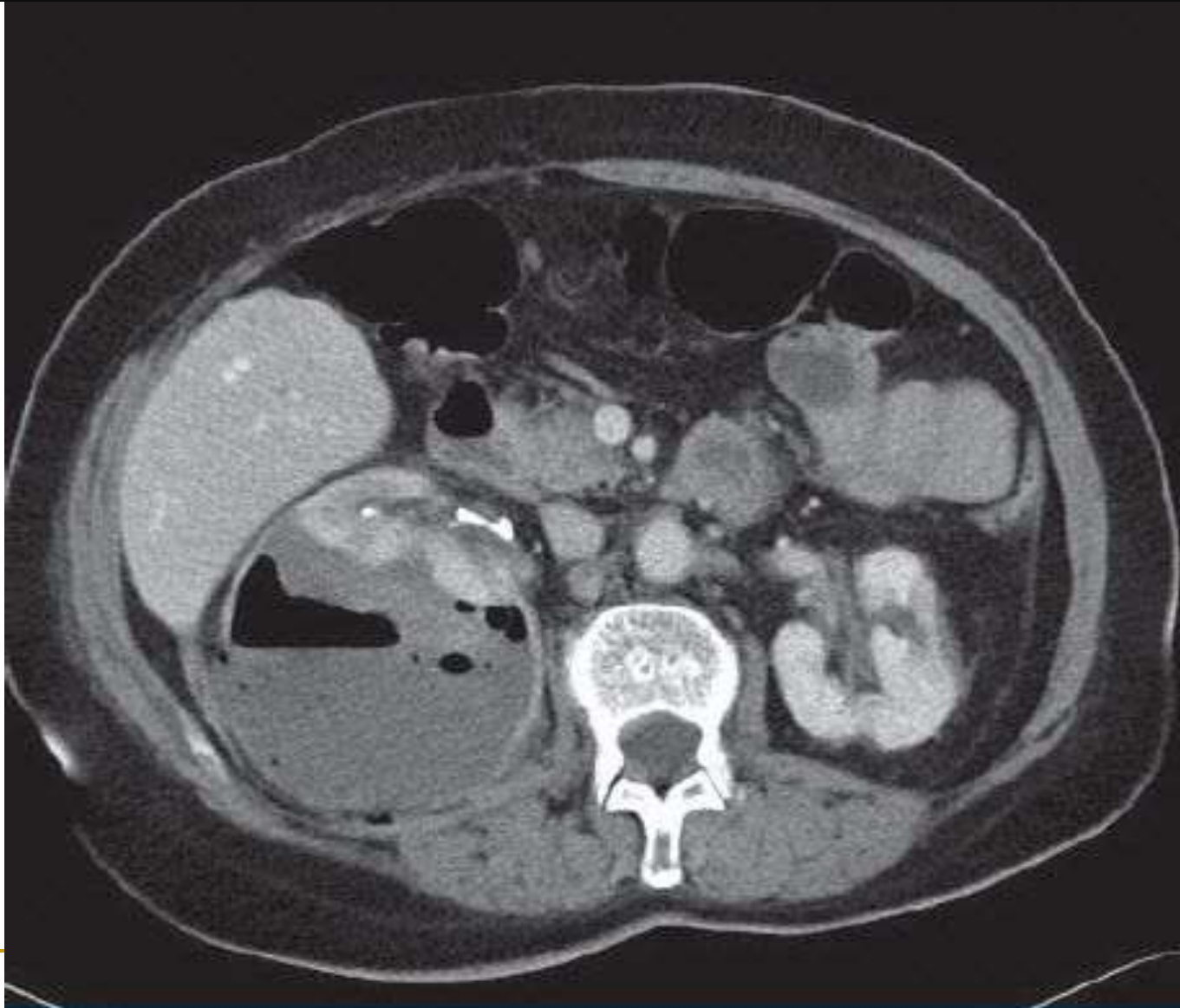
Emphysematous Pyelonephritis – 2

- 4 factors in pathogenesis: gas-forming bacteria, high tissue glucose, impaired tissue perfusion and a defective immune response
 - E. Coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Aerobacter aerogenes, Citrobacter and rarely yeast.
 - Left untreated, EPN is uniformly fatal
-

Emphysematous Pyelonephritis – 3

- Many of the earlier series have stressed the very high mortality rate (75%) and the need for urgent nephrectomy
- Estimates of mortality using current therapy range from 10% to 40%; 70% for medically versus 30% for surgically treated pts
- Thus, traditionally, it is thought that antibiotic therapy alone is usually ineffective, and prompt nephrectomy is necessary

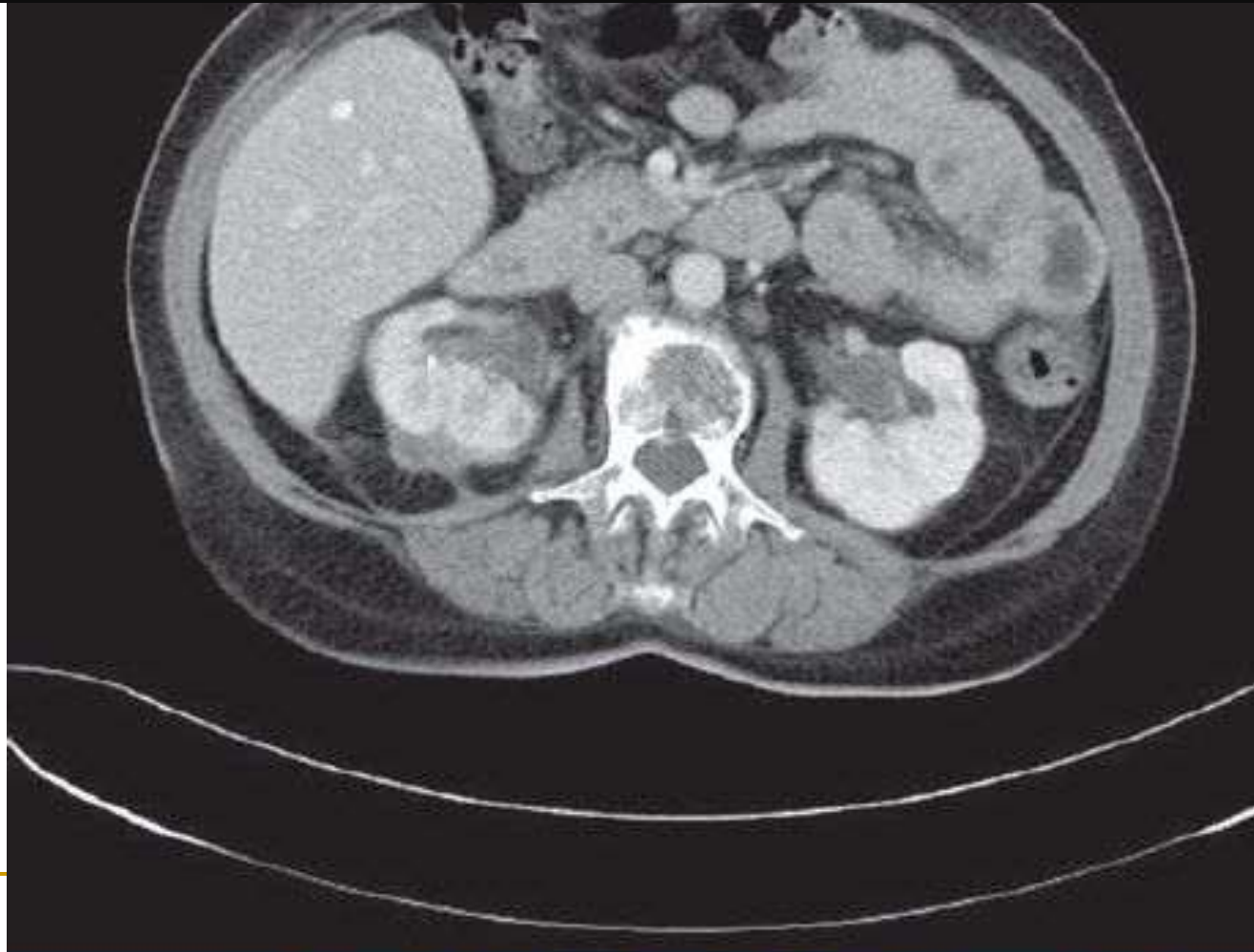
Contrast enhanced CT of abdomen showing large right-sided perinephric collection containing fluid and gas

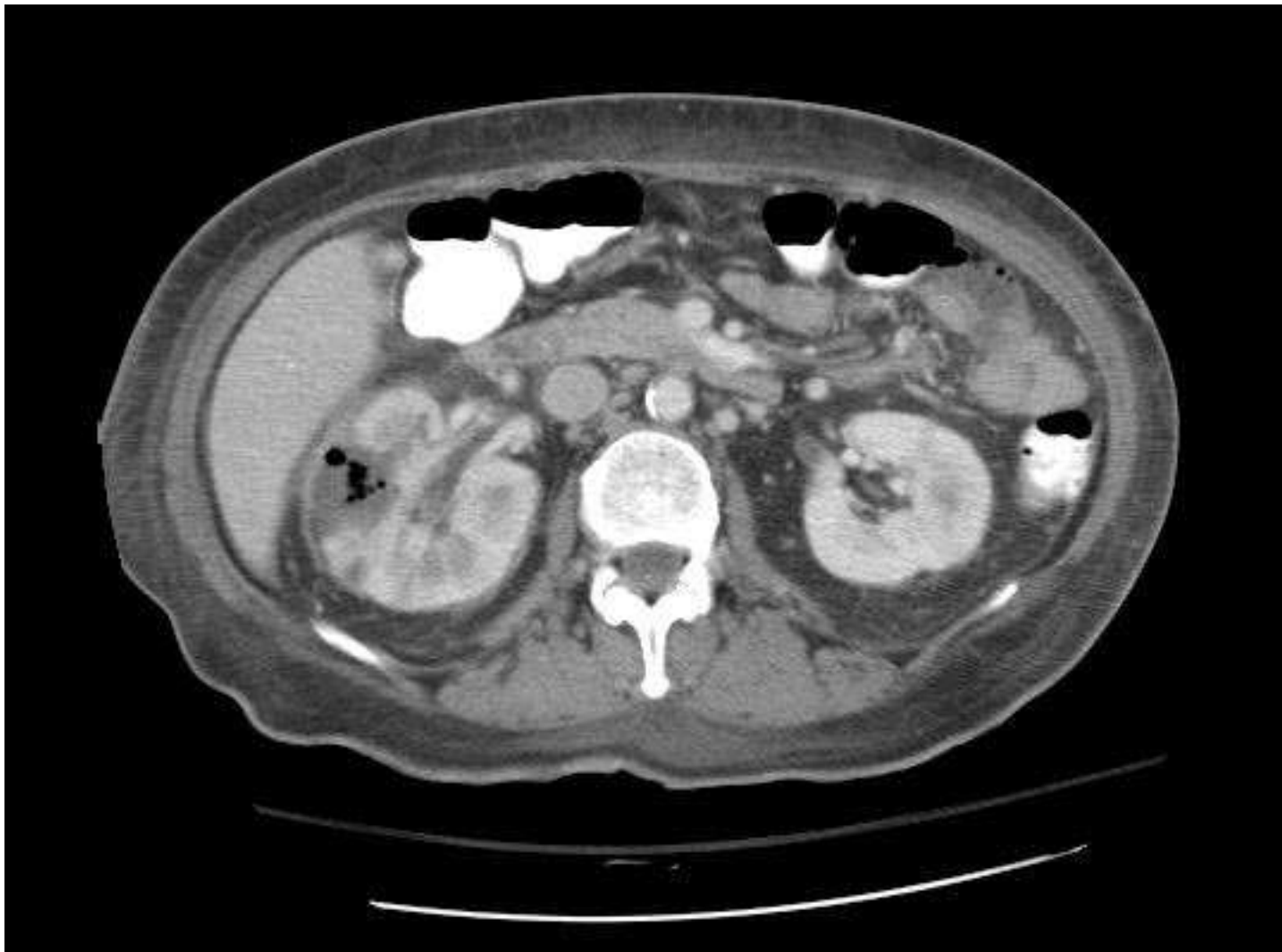


Repeat CT scan of abdomen with contrast showing marked improvement of the perinephric abscess with reduction in size of the collection 2 weeks after percutaneous drainage

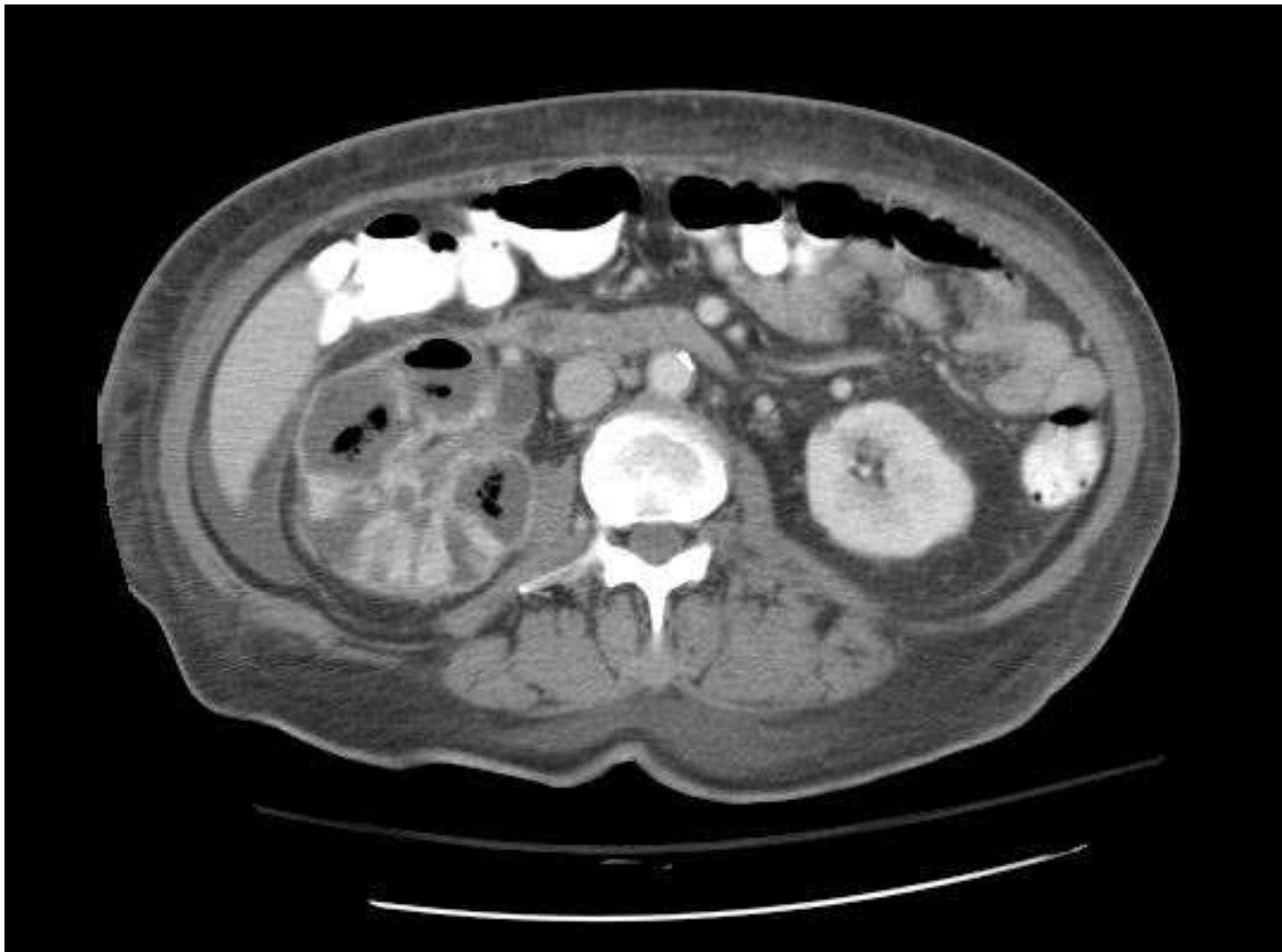


Repeat CT scan 3 months later showing marked improvement with significantly smaller residual collection around the right kidney which was thought to represent a haematoma





Emphysematous-pyelonephritis



Emphysematous-pyelonephritis



Emphysematous-pyelonephritis

Treatment of Tuberculosis in Renal Failure

- Rifampicin and isoniazid not cleared by dialysis.
- Give pyridoxine.
- Ethambutol not dialyzed. Reduce dose if glomerular filtration rate (GFR) <30 mL/min.
- Avoid rifampicin with cyclosporine.



Thank

You